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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/816,591	04/01/2004	Laura Fuertes-Lopez	NHL-NP-46	8510

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/09/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/816,591	FUERTES-LOPEZ ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-23* is/are pending in the application.

4a) Of the above claim(s) *19-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and response received on 1/25/07 has been entered. Claims 1-18 have been canceled and new claims 19-23 have been added. Claims 19-23 are currently pending in the instant application.

Newly submitted claims 19-21 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons: the original claims were drawn to DNA expression constructs, not methods of making DNA expression constructs, or methods of using DNA expression constructs. Previously pending claims 1-5, 7-8, 14-18 were drawn to DNA expression constructs or vaccines comprising DNA expression constructs. Claims 6, and 9-13 were drawn to "use" of the DNA expression construct.. However, as indicated in the previous office action, "use" claims, such as previous claims 6, and 9-13, are not considered proper method or process claims as the claims contain no actual method steps. As such, no methods were in fact claimed in the previous claim set. It is further noted that previous office action clearly indicated that despite the indefiniteness of the previous claims, in the interests of compact prosecution, search and examination of the previous claims would be based on products comprising a DNA expression construct or vaccine comprising a DNA expression construct, see page 7, last paragraph of the previous office action. Had the original claim set included methods of vaccinating as now claims in claims 19-20, or methods of making a vaccine as now claimed in claim 21, these claims would have been subject to restriction. Specifically, while the vaccines comprising a DNA expression construct and the methods of making a vaccine are related as process of making and product made, the inventions are distinct if either or both of the following

can be shown: (1) that the process as claimed can be used to make another and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case, the methods are drawn specifically to constructing a particular plasmid pMOK p36 and attaching an NLS peptides comprising PKKKRKV. However, the vaccines do not require this method as they can be made using other plasmids and NLS peptides. Further, while the vaccines and the methods of vaccinating a living being are related as product and process of use, the inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the vaccines can be used to transfect cells in vitro in tissue culture and further used to produce the p36 polypeptide in vitro. In addition, the methods of making the vaccine and the methods of using the vaccine do not share any method steps in common and thus have materially different designs and modes of operation. As such, the search and examination for each of the vaccine product, the method of making a vaccine, and a method of vaccinating a living being is not coextensive and it would place an undue burden on the examiner to search and examine all inventions together. Therefore, because these inventions are independent or distinct for the reasons given above and there would be a serious burden on the examiner if restriction is not required because the inventions have acquired a separate status in the art due to their recognized divergent subject matter, different classification and different search requirements, restriction for examination purposes as indicated is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 19-21 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 22-23 are currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in the previous office action.

Priority

The previous office action acknowledged applicant's claim for foreign priority based on applications filed in Germany on October 2, 2001 or November 12, 2001, but noted that certified copies of the DE 101 48 732.0 or DE 101 56 679.4 applications as required by 35 U.S.C. 119(b) had not been provided. In response, the applicant provided a certified copy of DE 101 56 679.4 in German. However, for DE 101 48 732.0, the office has only received a single cover page. A complete certified copy of DE 101 48 732.0 is required to fully comply with 35 U.S.C. 119(b).

Specification

The objection to the abstract of the disclosure is withdrawn in view of applicant's submission of a new abstract which does not contain improper legal language.

The objection to the disclosure for informalities on page 21, paragraph 4, is withdrawn in view of applicant's amendment to this section.

Nucleic acid and/or Amino acid Sequences

Applicant's amendment to the specification and claim amendments places this application in compliance with the requirements of 37 CFR 1.821 through 1.825.

Double Patenting

The provisional rejection of claims 1-18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 7-11, and 17-20 of copending Application No. 10/816,465, hereafter referred to as the '465 application, is withdrawn over canceled claims 1-18 and maintained over new claims 22-23 over new claims 29-31 of the '465 application.

The applicant argues that the cancellation of claim 1-18 and submission of new claims renders the present rejection moot as the new claims are patentably distinct from the claims of the '465 application. This is not agreed. The claims currently pending in the copending application 10/816,465 are still broadly drawn to a vaccine comprising a DNA expression construct to elicit a Th1 type immune response. While the instant claims are more narrow and drawn specifically to vaccines comprising the constructs for immunization against leishmania, and further limit the construct coding sequence to encoding the p36 LACK antigen and the oligopeptide to PKKKRKV, the '465 claims are broad and encompass the instant species. As indicated in the previous office action, while the '465 claims are broad and not limited to these

species, the '465 specification clearly teaches immunization against leishmania as a preferred embodiment and further the use of the p36 LACK antigen in the construct and the use of the PKKKRKV peptide ('465 specification, pages 4, 7, and 9). The broader claims of the '465 application in combination with the '465 applications disclosure render the narrower instant claims obvious. The rejection of record therefore stands.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The rejection of 6, and 9-13 under 35 U.S.C. 112, second paragraph and 35 U.S.C. 101 is withdrawn in view of the cancellation of these claims.

The rejection of claims 1-18 under 35 U.S.C. 112, second paragraph, for indefiniteness is withdrawn in view of the cancellation of these claims.

Claim Rejections - 35 USC § 103

The rejection of claims 1-18 under 35 U.S.C. 103(a) as being unpatentable over Gurunathan et al. 91997) J. Exp. Med., Vol. 186(7), 1137-1147, in view of U.S. Patent No. 6,451,593 (2002), hereafter referred to as Wittig et al., is withdrawn over canceled claims 1-18 and maintained over new claims 22-23. Applicant's arguments have been fully considered but

have not been found persuasive in overcoming the rejection of record as discussed in detail below.

The claims as amended recite a vaccine comprising a DNA expression construct for immunizing against leishmania where the DNA expression construct is a covalently closed linear DNA molecule comprising a linear double stranded region comprising a terminator sequence, and a coding sequence encoding p36 LACK under control of a promoter, where the single strands forming the double strand are linked a short single stranded loops of DNA, and where the construct is covalently linked to an oligopeptide. The applicant further claims said construct wherein the oligopeptide comprises PKKKRKV.

The applicant argues that the rejection of record does not meet the requirements for establishing a case of *prima facie* obviousness as set forth in MPEP 2143 over new claims 19-23. Please note that arguments addressing claims 19-21 are moot as these claims are withdrawn and have not been examined. Regarding claims 22-23, the applicant specifically argues that neither Wittig nor Gurunathan teach or suggest the limitations of these new claims.

In response, this is not agreed as the combination of Gurunathan and Wittig does in fact teach and suggest all the particular limitations in new claims 22-23. The teachings of both references as set forth in the previous office action and as they apply to new claims 22-23 are reiterated as follows. Gurunathan et al. teaches a DNA expression construct encoding the p36 LACK antigen from *Leishmania major* operatively linked to the CMV promoter and a polyA sequence and a vaccine comprising the expression construct for generating protective immunity against *Leishmania major* in a mammal (Gurunathan et al., pages 1137-1139). Please note that the polyA sequence is a "terminator" sequence.

Gurunathan et al. differs from the instant invention in that the DNA expression construct is plasmid and in that the DNA is not covalently linked to an oligopeptide such as PKKKRKV. Wittig et al. supplements Gurunathan et al. by teaching dumbbell shaped DNA expression constructs comprising covalently closed linear DNA that contains only a coding sequence operably linked to a promoter and polyA termination sequence where the linear ends are linked by short single stranded loops of DNA, and wherein the construct is further covalently linked to a peptide which directs transport of the construct across a cell's endosome or into the nucleus (Wittig et al., claims 1-11, and columns 5-8)). In particular, Wittig et al. specifically teaches the use of the nuclear localization sequence (NLS) from SV40, a sequence which inherently comprises PKKKRKV (Wittig et al., column 5). Wittig et al. also teaches a vaccine comprising this construct for treating infectious diseases (Wittig et al., columns 1 and 8). Wittig et al. further provides motivation for using a dumbbell DNA expression construct linked to a peptide over a plasmid DNA expression construct. Wittig et al. teaches that because the dumbbell construct consists only of a promoter-gene-terminator sequence, these constructs have none of the disadvantages of plasmid constructs, which include their size, which inhibits fast transport into the cell's nucleus, and the presence of unwanted background sequences, including bacterial sequences, which can lead to unintended immune responses (Wittig et al., columns 2-3, bridging paragraph). Therefore, based on the advantages to using dumbbell DNA expression constructs over plasmid constructs for immunization, it would have been *prima facie* obvious to the skilled artisan at the time of filing to use a dumbbell DNA construct encoding p36 LACK linked to a peptide according to the teachings of Wittig instead of a plasmid construct in the methods of immunizing against Leishmania taught by Gurunathan et al. Further, based on the substantial

guidance for making dumbbell constructs provided by Wittig et al., the skilled artisan would have had a reasonable expectation of success in making a dumbbell DNA expression construct encoding the p36 LACK antigen covalently linked to a peptide such as the NLS peptide from SV40. Thus, from the above, it is clear that in fact the combination of Gurunathan et al. and Wittig et al. teaches and suggest the exact limitations of the vaccines recited in new claims 22-23.

The applicant further argues that there would be no reasonable expectation of success in combining the teachings of Wittig and Gurunathan because in applicant's opinion, " ..the art of biology and genetics is very unpredictable. It is extremely difficult, if not impossible, to have any reasonable expectation of success when combining teachings." In response, this argument is not persuasive. According to applicant's conception of the state of art of biology and genetics, it would be impossible to have any reasonable expectation of success in combining the teachings of any references relating to biology. If such were the case, no 103 rejections could be made or sustained over any claims with subject matter in the fields of biology of genetics. However, this is not the case. A quick review of published Court decisions both predating and postdating the effective filing date of the instant application, both from the Federal Circuit and the Board of Appeals and Interferences, will show that there is plenty of case law which upholds 103 rejections over claims relating to biology, molecular biology, genetics, and cellular biology. Further, regarding the potential efficacy of any vaccine made to treat Leishmaniasis, it is noted that the claims under examination are product claims. Further, Gurunathon et al. clearly teaches the successful use of plasmids encoding p36 LACK antigen to generate protective immunity against Leishmaniasis. Given the clear teachings of Wittig et al. that the dumbbell constructs

encoding infectious antigens have substantial advantages of plasmids, the skilled artisan would have had both motivation and a more than reasonable expectation of being successful in making a vaccine comprising a construct as claimed encoding p36 LACK.

Finally, the applicant argues that the rejection is based on improper hindsight reasoning. In response, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). As illustrated above, the specific motivation to combine the teachings of Gurunathon with those of Wittig was specifically provided by Wittig et al. who teaches the substantial advantages of dumbbell constructs over plasmids for making vaccines. Therefore, applicant's arguments are not found persuasive and the rejection of record stands over new claims 22-23.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

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PRIMARY EXAMINER